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10/511,101	09/12/2005	R. Rao Koganty	KOGANTY 4A	6156

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,101	KOGANTY ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2008*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 2, 8, 10-24, 26-81, 87-90, 134-140* is/are pending in the application.

4a) Of the above claim(s) *75,76,81 and 134-137* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,8,10-15,18,19,21-24,30-46,49-51,70,72,77-80,87-90 and 138* is/are rejected.

7)☒ Claim(s) *16,17,20,26-29,47, 48, 52-69,71,73,74,139 and 140* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/08 and 2/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 2/13/2008 is acknowledged. The traversal is on the ground(s) that the amendment of the claim 1 to recite a glycolipopeptide comprising at least two MUC1 peptide epitopes distinguishes the claimed glycolipopeptides from the teachings of the prior art relied upon by the USPTO, and that relied upon by the EPO (which applicant discusses in the traverse). Additionally, applicants elect the species of glycolipopeptides comprising at least one MUC1-associated epitope, and wish clarification of the species restriction. Specifically, if applicants elect MUC1 epitope, does this limit them to glycolipopeptides having only MUC1 epitopes? In the present case, given that the claims have been amended, it appears that the correct interpretation of the species election, is that the search and examination of the claimed glycolipopeptpides will be begin with the species of glycolipopeptides having at least 2 MUC1 peptide epitopes, and that claims drawn to glycolipopeptides having at least 2 MUC1 peptide epitopes and, in addition, other epitopes are considered within the scope of the elected species (e.g. claims drawn to glycolipopeptides comprising at least two MUC1 peptide epitopes and further comprising epitopes such as the Tn or STn epitopes will be searched and examined). With respect to the argument for rejoining the product claims with the method claims, this is not found persuasive because the amendment to the claims does not distinguish the claims from the prior art. In the original restriction requirement, the feature linking invention groups I and II was a glyolipopeptide comprising at least 5 amino acids, at least one amino aid being a glycosylated amino acid and at least one

amino acid being a lipidated amino acid, where at least one lipidated amino acid is an interior amino acid and the glycolipopeptide comprises at least one disease-associated epitope. Applicants assert that the present claims are distinguished from the prior art because they are limited to glycolipopeptides comprising at least two MUC1 peptide epitopes, and that there is no motivation to lipidate Karsten's glycopeptides or to glycosylate Zeng's lipopeptides, even if either of these references taught peptides with at least two MUC1 peptide epitopes. In response, it is noted that Finn (US 5,744,144; issued 4/28/1998; cited in the IDS) teaches the concept of synthetic MUC-1 peptides comprising at least two 20-amino acid tandem repeats of MUC-1 (see abstract). Therefore, it would have been obvious to make a tandem repeat of Karsten's glycopeptide in view of the teachings of Finn, and further to lipidate Karsten's glycopeptides in view of Zheng because Zheng teaches that synthetic lipopeptides with built-in lipophilic advent Pam_3Cys, where the Pam_3Cys is linked to an interior amino acid (see abstract and page 68). Thus, the structure of claim 1 does not appear to be a special technical feature that makes a contribution over the prior art, and is not a special technical feature that links groups I and II. The restriction between groups I and II is maintained.

The requirement is still deemed proper and is therefore made FINAL.

In view of the restriction between groups I and II, Applicants are reminded of *In re Ochiai*:

Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable**

product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Objections

Claims 134-137 are objected to for depending from claim 1, drawn to a glycolipopeptide, but reciting "method of claim 1". Therefore, claims 134-137 are withdrawn from consideration.

Claims 1, 2, 8, 10-24, 26-81, 87-90, 134-140 are pending.

Claims 75, 76, 81 and 134-137, drawn to non-elected inventions, are withdrawn from consideration.

Claims 1, 2, 8, 10-24, 26-74, 77-80, 87-90 and 138-140 are examined on the merits.

Claim Objections

Claims 8, 11, 13, 47, 48, 87 and 89 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 8, 11, 13 depend from claim 1, which recites a glycolipopeptide comprising at least two MUC 1 peptide epitopes, whereas claim 8, recites a glycolipopeptide that comprises at least one T cell epitope; claim 11 recites a glycopeptide that comprises the amino acid sequence PDTRP; claim 13 recites a glycolipopeptide that comprises the sequence SAPDTRP; claim 87 recites a glycopeptide that comprises the amin oacid sequence PDTRP; and claim 89 recites a glycolipopeptide that comprises at least one copy of the MUC1 consensus tandem repeat. Because these claims refer to the claimed glycolipopeptide as glycopeptides (claims 11 and 87), comprising only one MUC1 epitope, but claim 1 requires at least 2 MUC1 epitope, claims 8, 11, 13, 87 and 89 fail to further limit claim 1. Claims 47 and 48 recite "the amino terminal amino acid" or "the carboxy terminal amino acid" comprising a strongly lipophilic group, when claim 1 requires that an internal amino acid is lipidated.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 8, 11, 36-46, 62-64, 68-70 and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite because of the phrase "where at least one epitope is a cancer-associated epitope other than a MUC1 peptide epitope". Because claim 1 requires at least two MUC 1 peptide epitopes, it is not clear if, in claim 2, one of the MUC 1 peptide epitopes is substituted with a non-MUC 1 epitope, or if the non-MUC 1 epitope is in addition to the at least two MUC 1 peptide epitopes recited in claim 1. At least one of what?

Claim 8 is indefinite because of the phrase "which comprises at least one T cell epitope." Is the T cell epitope of claim 8 one of the at least two MUC 1 peptide epitopes, or an additional epitope?

Claims 11 and 87 are indefinite because the phrase "the glycopeptide" lacks antecedent basis in claim 1.

Claims 36 and 37 are indefinite because the phrase "said group" lacks antecedent basis in claim 1.

Claims 38-46 are indefinite because the phrase "at least one strongly lipophilic group" in claim 38 lacks antecedent basis in claim 1. This rejection may be obviated by amending to the

following: "wherein the at least one lipidated amino acid has at least one strongly lipophilic group with a logP, as predicted by the Meylan algorithm of at least 2.7".

Claims 62-64, 68 and 69 are indefinite because they recite a moiety of the form –A'-Y'-Z', where the only definition provided is that A', Y' and Z' are defined "analogously" to A, Y and Z, respectively. Does this mean that A = A', Y = Y' and Z= Z'?

Claims 70 and 72 are indefinite because the phrase "the strongly lipophilic group of at least one lipidated amino acid" lacks antecedent basis in claim 1.

Claims 73 and 74 are indefinite because the structure pictured is identified as having the amino acid sequence of SEQ ID NO: 2, but carboxy terminus of SEQ ID NO: 2 contains "GVSSL", whereas the structure pictured does not show the two serine residues between V and L, but instead indicates that "Lipids" refers to two or more consecutive lapidated amino acids. Does this mean that what is pictured is showing a structure which may have any amino acid between V and L at the carboxy terminus?

Claim 88 is indefinite because the phrase "the glycolipopeptide" lacks antecedent basis in claim 87.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification lacks an adequate written description and exemplification of MUC1 T cell epitopes.

The claimed inventions are drawn to glycolipopeptides comprising at least one MUC1 T cell peptide epitope. This is construed to mean that the claimed glycolipopeptides should be capable of eliciting a T cell lytic response. The specification provides one example of the structure of a MUC1 T cell epitope, that of SAPDTRP. The specification also describes methods for determining possible T cell epitopes. However it appears that the theoretical methods for determining T cell epitopes in polypeptides do not correspond to discovering actual T cell epitopes, or describing actual T cell epitope structures. Therefore, the specification has failed to provide an adequate written description of the genus of MUC 1 T cell epitopes. U.S. Patent 5,840,839 (issued Nov. 24, 1998) teaches that finding a peptide that binds to an MHC molecule and stimulates an immune response is not a trivial matter, and that despite the existence of methods for predicting theoretical T cell epitopes, success in finding a structure of T cell epitope is not readily predictable. In the '839 patent (col. 19-20, and Table 1), data is shown that illustrates that a series of theoretical T cell epitopes that were derived based on a binding motif of MHC molecule HLA-A31 did not elicit a T cell lytic response when they are tested. These results suggest that theoretically selected T cell binding motifs have to be tested experimentally in order to determine whether they are actually T cell epitopes or not. While the specification provides one example of a MUC 1 T cell epitope, the specification fails to provide any other examples, and to demonstrate that any theoretical T cell epitopes elicit a T cell lytic response.

Because US 5,840,839 teaches that finding T cell epitopes is unpredictable, it does not appear that the specification has provided a description for how to make the genus of MUC 1 T cell epitopes that are encompassed by the claims. Therefore, one of skill in the art would not find that applicant is in possession of the inventions as broadly claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 8, 10-15, 18, 19, 21, 22-24, 30- 35, 49, 51, 70, 87-90, and 138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livingston (WO 97/34921; published 25 September 1997) in view of Zeng (Zheng, W. et al., J. Peptide Science, 2: 66-72, 1996; of record) and further in view of Karsten (Karsten, U. et al., Cancer Research, 58: 2541-2549, 1998).

Livingston teaches a peptide comprising at least two MUC 1 epitopes (see claims 7 and 8 for example). Livingston fails to teach peptides that are both glycosylated and lipididated, where at least one internal amino acid is lipidated. However, Zeng teaches the construction of peptide vaccines with Pam3Cys as a built in adjuvant. Pam3Cys is tripalmitoyl-S-glyceryl cysteine. In Zeng's example, the Pam3Cys is attached to an internal amino acid. Zeng teaches that constructing a peptide antigen with a built in adjuvant may allow one to make an adjuvant-free vaccine, allowing the avoidance of the side effects associated with many known adjuvants (see page 71, left column and page 68-69). Additionally, Karsten teaches that antigencity of the DTR motif of the MUC1 epitope is increased by glycosylation with the TF and Tn antigens within the DTR motif (see abstract; page 2541, right column). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the peptides of Livingston, which comprise at least two MUC 1 peptide epitopes, by using the method of Zeng to construct a peptide with Pam3Cys groups attached to a lysine to make a built in adjuvant, and by using the method of Karsten to glycosylate the peptide. Zeng teaches that advantages of lipidating amino acid residues, and Karsten teaches the advantages of

glycosylating amino acid residues. In both cases the immunogencity of the synthetic peptide is increased. Thus, the teachings of Zeng and Karsten provide motivation for combining the references to make the claimed inventions.

Claims 1, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livingston (WO 97/34921; published 25 September 1997) in view of Zeng (Zheng, W. et al., J. Peptide Science, 2: 66-72, 1996; of record); in view of Karsten (Karsten, U. et al., Cancer Research, 58: 2541-2549, 1998); and further in view of Boutillon (US 5,871,746; issued Feb. 16, 1999).

Claim 50 recites that the lapidated amino acid is lipidated Ser or Thr. The combination of Livingston, Zeng and Karsten teach a lipidated Lys residue. However, the attachment of Pam3Cys to peptides via Ser is known in the prior art as evidenced by the teachings of Boutillon (see column 1, lines 46-57). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a serine residue instead of the lysine residue of Zeng to make a lipidated glycopeptide as claimed. The use of serine and lysine appear to be equivalent.

Claims 1, and 77-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Livingston (WO 97/34921; published 25 September 1997) in view of Zeng (Zheng, W. et al., J. Peptide Science, 2: 66-72, 1996; of record); in view of Karsten (Karsten, U. et al., Cancer Research, 58: 2541-2549, 1998; of record); and further in view of Guan (Guan, H.H. et al., Bioconjugate Chem., 9: 451-458, 1998).

Claims 77-80 recited compositions comprising the glycolipopeptide of claim 1 and a liposome. The use of liposomes to modulate immune response to lipidated peptide antigens is known in the art as evidenced by the teachings of Guan (see abstract). The liposomes of Guan comprising phosphatidyl choline, cholesterol and phosphatidyl glycerol (see page 452, left column). Guan teaches hydrophilic MUC 1 peptides are unlikely to associate with the lipid bilayer of a liposome, whereas antigens containing hydrophobic domains may physically associate with the lipid bilayers. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have combined the lipidated glyopeptides taught by the combination of Livingston, Zeng and Karsten, because the use of liposomes in the vaccine arts is well known, and because Guan teaches that modification of liposomes can be use to alter immune responses to peptide antigens (see page 457).

Conclusion

Claims 1, 2, 8, 10-15, 18, 19, 21-24, 30-46, 49-51, 70, 72, 77-80, 87-90 and 138 are rejected. Claims 16, 17, 20, 26-29, 47, 48, 52-69, 71, 73, 74, 139 and 140 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the

status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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Patent Examiner
September 15, 2008
/Alana M. Harris, Ph.D./
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